

REPLACEMENT SHEET

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Title: RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY,
THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES

Applicants: Rene Gantier et al. Attorney Docket No. 17109-012001/922

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Cytokine regions susceptible to protease attack identified by structural alignment with Lead mutants

of IFN α -2b

IFN- α 2b CDLPQTHSLGSRRTIMLLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQAKETIPVLHEMIQOIFNLFSTKDSAAWDETLDDKPYTELXQOLNDLEACVLIQG

VGVTETPLMKEDSIIAVRKYRQRTITYLKEKKYSPCAMEVVRRAETMRSPSLSTNIQESLRSE

Exemplary protein of the interferons/interleukin-10 family

IFN- β MSYNLIGFLQSSNFQCCOKLMQNLGRLEYCLKDRMNPDIPEETKQLOQFQKEDALTIYENLQNIFAIFRODSSSTGNNETIVENLLANVYHQINHLKTVLEEK

LEKEDPTRGKLMSLHLKRYGRILHYLKAKEYSHCAWTIVRVEILLRNFYFINRLTGYLRN

Exemplary protein of the short-chain cytokines family

EPO APPRLICDSRVLEERYLLAKEAENITTTGCAHCSLNENITVPDTEVNFYAKRMEYGOQAVEVWQGLALLSEAVLRGQALLVNSSQPMWEPLOLHVDAKAVSGURSL

TTLLRGAQKEAISPDDAASAPLRTITADTFPRKLFRRVSNFLRGKLLKLYTGEACRTGDR

Exemplary protein of the long-chain cytokines family

G-CSF TPLGPASSLPQSFLKLCLEQVRKIQDGDALQEKLVSECATYKLCHEPELVLLGHSIGIPWAPLSSCPSQALQLAGCLSQLHSGLPFLYQGLLQALEGISPEIGPTLDTLOL

DVADFAITTIWQMEELGNAPALQPTQGANPAPASAFQRRAGGVLVASHLQSFLEVSRYVLRHLAQP

FIG. 9